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EXAMINER	
STEADMAN, DAVID J	
ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/543,046	SHEWCHUK ET AL.	
	Examiner	Art Unit	
	David J. Steadman	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *06 June 2007 and 14 April 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *4,6 and 10-14* is/are pending in the application.

4a) Of the above claim(s) *11-14* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *4,6 and 10* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☒ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/6/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the Application

[1] Claims 4, 6, and 10-14 are pending in the application.

Election/Restriction

[2] Applicant's election of Group II, original claims 4-6, in the response filed on 6/6/07 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

[3] Applicant's election with traverse of species iv, interaction with amino acid residue 799, in the reply filed on 4/14/08 is acknowledged. The traversal is on the ground(s) that "there is a technical relationship between species i-xxxi because they are all potential sites of interaction between the ErbB4 kinase domain and a compound that is a potential inhibitor. Accordingly, these species are linked to form a general inventive concept and should be examined together". Applicant further argues "at such time as the elected species is determined to be allowable, Applicants will request rejoinder of the remaining species". This is not found persuasive because according to PCT Rule 13.2 unity of invention exists only when the shared same or corresponding special technical feature is a contribution over the prior art. The species of i to xxxi do not relate to a single general inventive concept because they lack the same or corresponding special technical feature. The technical feature of species i to xxxi is a method of ErbB4 inhibitor design, which is shown by the combination of Groenen, Cohen, Traxler,

Plowman-1, and Plowman-2, and optionally in view of the legal rationale of *In re Gulack,* to lack novelty or inventive step because the combination teaches a method of ErbB4 inhibitor design for reasons set forth below and does not make it a contribution over the prior art.

The requirement is still deemed proper and is therefore made FINAL.

[4] Claims 11-14 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 4/14/08.

[5] Claims 6 and 10 are being examined only to the extent the claims read on the elected species.

Information Disclosure Statement

[6] With the exception of the reference of Cox et al., all references cited in the IDS filed on 6/6/07 have been considered by the examiner. See Form PTO/SB/08 attached to the instant Office action. The reference of Cox et al. has been lined through as the examiner can find no copy of the Cox et al. reference in the application file.

Claim to Domestic Priority

[7] Applicant's claim to domestic priority under 35 U.S.C. 119(e) to US provisional application 60/441,443, filed on 1/21/03, is acknowledged. Applicant's priority claim has been perfected in the preliminary specification amendment filed on 7/21/05.

Oath/Declaration

[8] The Declaration filed under 37 CFR 1.63 is objected to for listing the incorrect filing date for PCT/US04/01291. According to the Declaration, the PCT/US04/01291 application was filed on 12/20/04, however, according to USPTO records, the application was filed on 1/20/04. Appropriate correction is required.

Specification/Informalities

[9] The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: ---Method of Inhibitor Design using a 3-D structure of ErbB4 Kinase---.

[10] The specification is objected to as failing to comply with the requirements for a sequence listing. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF)

copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). See particularly specification pp. 44 and 55 and the disclosed Table 2 beginning at p. 59 of the specification containing a list of atomic coordinates representing the disclosure of an amino acid sequence. Applicant should identify the disclosed sequences by proper sequence identifiers.

Claim Rejections - 35 USC § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

[11] Claims 4, 6, and 10 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

[a] Claims 4, 6, and 10 are indefinite in the recitation of "…a three dimensional computer model which represents ErB4 kinase domain…has the structural coordinates of Table 2". In this case, the term "represent" has at least two meanings such that the scope of claim 4 is unclear. For example, "represent" in claim 4 can be interpreted as meaning that the recited 3-D model is a 3-D model of an ErbB4 kinase domain, wherein the 3-D model has the structural coordinates of Table 2. Alternatively, according to a dictionary definition of "represent" (obtained from www.merriam-webster.com/, last

viewed on 5/13/08), the term can be interpreted as meaning to serve as an example of something, such that the 3-D structure serves as an example of an ErbB4 kinase domain – but is not limited to having the structural coordinates of Table 2. In accordance with MPEP 2111, the examiner has adopted the latter interpretation of the term “represents”.

[b] Claim 4 is indefinite in the recitation of "evaluating compounds..." in step (b) as it is unclear from the claims and the specification as to what is encompassed by the term "evaluating" such that a skilled artisan would recognize the scope of those compounds that are selected for further testing in step (c). It is suggested that applicant clarify the meaning of the noted phrase.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

[12] Claim(s) 4, 6, and 10 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

According to MPEP 2163.II.A.1, in evaluating a claimed invention for adequate written description, the examiner should determine what the claim as a whole covers. “Claim construction is an essential part of the examination process. Each claim must be separately analyzed and given its broadest reasonable interpretation in light of and consistent with the written description. See, e.g., *In re Morris*, 127 F.3d 1048, 1053-54, 44 USPQ2d 1023, 1027 (Fed. Cir. 1997).”

The claims are drawn to methods of ErbB4 inhibitor design by "generating” a genus of 3-D computer models of ErbB4 kinase domain in liganded form. As noted above, the term “represents” has been broadly, but reasonably interpreted as meaning to serve as an example of something, such that the recited 3-D model serves as an example of an ErbB4 kinase domain – but is not limited to having the structural coordinates of Table 2. Put another way, the claims have been interpreted as meaning that the recited 3-D model is of an ErbB4 kinase domain, wherein the 3-D model is unlimited with respect to the structural coordinates that define the model.

Regarding the method of "generating” the recited 3-D model, the specification discloses (p. 12, bottom), “As used herein, the terms "structure coordinates" and "structural coordinates" are interchangeable and mean mathematical coordinates derived from mathematical equations related to the patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centers) of a molecule, for instance ErbB4K, in crystal form. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are used to establish the positions of the individual atoms within the unit cell of the crystal”. See also

pp. 55-56 of the specification, which discloses a method of “generating" a 3-D model of ErbB4 by crystallization and x-ray diffraction. In view of this disclosure, it appears that the term "generating" with respect to a 3-D model is intended to encompass obtaining structural coordinates by crystallization of an ErbB4 polypeptide or kinase domain thereof and has been interpreted accordingly.

MPEP 2163.II.A.2.(a).i) states, “Whether the specification shows that applicant was in possession of the claimed invention is not a single, simple determination, but rather is a factual determination reached by considering a number of factors. Factors to be considered in determining whether there is sufficient evidence of possession include the level of skill and knowledge in the art, partial structure, physical and/or chemical properties, functional characteristics alone or coupled with a known or disclosed correlation between structure and function, and the method of making the claimed invention”. For claims drawn to a genus, MPEP § 2163 states the written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant, identifying characteristics, *i.e.,* structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. MPEP § 2163 further states that a “representative number of species” means that the species which are adequately described are representative of the entire

genus. Thus, when there is substantial variation within the genus, one must describe a sufficient variety of species to reflect the variation within the genus.

In this case, the specification discloses only a single representative species of ErbB4 kinase domain 3-D models, *i.e.,* ErbB4 kinase domain 3-D model having the structural coordinates of Table 2 and, to the extent the “generating” step encompasses crystallography, only a single method for "generating” such a model, *i.e.,* the method set forth at pp. 44-47 and 55-56. Other than these species, the specification fails to disclose any other species of ErbB4 kinase domain 3-D models or methods of "generating" such models by crystallography. Given the lack of description of a representative number of species, the specification fails to sufficiently describe the claimed invention in such full, clear, concise, and exact terms that a skilled artisan would recognize that applicant was in possession of the claimed invention.

[13] Claims 4, 6, and 10 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of identifying potential ErbB4 kinase inhibitors using a 3-D model of ErbB4 having the structural coordinates of Table 2, does not reasonably provide enablement for all methods of inhibitor design as broadly encompassed by the claims. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

According to MPEP 2164, “[t]he purpose of the requirement that the specification describe the invention in such terms that one skilled in the art can make and use the

claimed invention is to ensure that the invention is communicated to the interested public in a meaningful way. The information contained in the disclosure of an application must be sufficient to inform those skilled in the relevant art how to both make and use the claimed invention". "The test of enablement is not whether any experimentation is necessary, but whether, if experimentation is necessary, it is undue." *In re Angstadt*, 537 F.2d 498, 504, 190 USPQ 214, 219 (CCPA 1976). Factors to be considered in determining whether undue experimentation is required are summarized in *In re Wands* (858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988)) as follows: (A) The breadth of the claims; (B) The nature of the invention; (C) The state of the prior art; (D) The level of one of ordinary skill; (E) The level of predictability in the art; (F) The amount of direction provided by the inventor; (G) The existence of working examples; and (H) The quantity of experimentation needed to make or use the invention based on the content of the disclosure. See MPEP § 2164.01(a). The Factors most relevant to the instant rejection are addressed in detail below.

The breadth of the claims: According to MPEP 2164.04, "[b]efore any analysis of enablement can occur, it is necessary for the examiner to construe the claims…and explicitly set forth the scope of the claim when writing an Office action." Also, MPEP 2164.08 states, "[w]hen analyzing the enabled scope of a claim, the teachings of the specification must not be ignored because claims are to be given their broadest reasonable interpretation that is consistent with the specification."

The claims are drawn to methods of ErbB4 inhibitor design by "generating" a genus of 3-D computer models of ErbB4 kinase domain in liganded form. As noted

above, the term “represents” has been broadly, but reasonably interpreted as meaning to serve as an example of something, such that the recited 3-D model serves as an example of an ErbB4 kinase domain – but is not limited to having the structural coordinates of Table 2. Put another way, the claims have been interpreted as meaning that the recited 3-D model is of an ErbB4 kinase domain, wherein the 3-D model is unlimited with respect to the structural coordinates that define the model.

Regarding the method of "generating” the recited 3-D model, the specification discloses (p. 12, bottom), “As used herein, the terms "structure coordinates" and "structural coordinates" are interchangeable and mean mathematical coordinates derived from mathematical equations related to the patterns obtained on diffraction of a monochromatic beam of X-rays by the atoms (scattering centers) of a molecule, for instance ErbB4K, in crystal form. The diffraction data are used to calculate an electron density map of the repeating unit of the crystal. The electron density maps are used to establish the positions of the individual atoms within the unit cell of the crystal”. See also pp. 55-56 of the specification, which discloses a method of “generating" a 3-D model of ErbB4 by crystallization and x-ray diffraction. In view of this disclosure, it appears that the term "generating" with respect to a 3-D model is intended to encompass obtaining structural coordinates by crystallization of an ErbB4 polypeptide or kinase domain thereof and has been interpreted accordingly.

The amount of direction provided by the inventor; The existence of working examples: The specification discloses only a single working example of ErbB4 kinase domain 3-D models, *i.e.,* ErbB4 kinase domain 3-D model having the structural

coordinates of Table 2 and, to the extent the "generating" step encompasses crystallography, only a single method for "generating" such a model, *i.e.,* the method set forth at pp. 44-47 and 55-56. Other than these disclosed working examples, the specification fails to disclose any other working examples of ErbB4 kinase domain 3-D models or methods of "generating" such models by crystallography.

The state of the prior art; The level of one of ordinary skill; and The level of predictability in the art: The state of the art at the time of the invention acknowledges a high level of unpredictability for making a protein crystal. For example, the reference of Branden et al. ("Introduction to Protein Structure Second Edition", Garland Publishing Inc., New York, 1999) teaches that "[c]rystallization is usually quite difficult to achieve" (p. 375) and that "The first prerequisite for solving the three-dimensional structure of a protein by x-ray crystallography is a well-ordered crystal that will diffract x-rays strongly…[w]ell-ordered crystals…are difficult to grow because globular protein molecules are large, spherical, or ellipsoidal objects with irregular surfaces, and it is impossible to pack them into a crystal without forming large holes or channels between the individual molecules" (p. 374). Also, Drenth et al. ("Principles of X-ray Crystallography," Springer, New York, 1999) teaches that "[t]he science of protein crystallization is an underdeveloped area" and "[p]rotein crystallization is mainly a trial-and-error procedure" (p. 1). One cannot predict *a priori* those conditions that will lead to the successful crystallization of a diffraction-quality crystal nor can one predict the space group symmetry or unit cell dimensions of the resulting crystal. See Kierzek et al. (*Biophys Chem* 91:1-20), which teaches that "each protein crystallizes under a unique

set of conditions that cannot be predicted from easily measurable physico-chemical properties" and that "crystallization conditions must be empirically established for each protein to be crystallized" (underline added for emphasis, p. 2, left column, top). Also, Wiencek (*Ann Rev Biomed Eng* 1:505-534) teaches that "[p]rotein solubility will change dramatically as pH is altered by ~ 0.5 pH units…some systems are sensitive to pH changes as small as 0.1 pH units" (p. 514, bottom). See also the teachings of McPherson (*supra*), which states (p. 13, column 2), "Table 2 lists physical, chemical and biological variables that may influence to a greater of less extent the crystallization of proteins. The difficulty in properly arriving at a just assignment of importance for each factor is substantial for several reasons. Every protein is different in its properties and, surprisingly perhaps, this applies even to proteins that differ by no more than one or just a few amino acids." Table 2 is a list of 25 different variables that can or do affect protein crystallization. As McPherson points out trying to identify those variables that are most important for each protein is extremely difficult and changing a protein by even a single amino acid can result is significant influences upon the change in which variables are important for successful crystallization. McPherson also goes on to teach, "[b]ecause each protein is unique, there are few means available to predict in advance the specific values of a variable, or sets of conditions that might be most profitably explored. Finally, the various parameters under one's control are not independent of one another and their interrelations may be complex and difficult to discern. It is therefore, not easy to elaborate rational guidelines relating to physical factors or ingredients in the mother liquor that can increase the probability of success in crystallizing a particular protein.

The specific component and condition must be carefully deduced and refined for each individual." Thus, in view of these teachings, a skilled artisan would recognize there is a high level of unpredictability in making a protein crystal, *e.g.,* a crystal of ErbB4 kinase domain.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure: While methods of protein crystallography were known in the art at the time of the invention, it was not routine in the art to screen all polypeptides, optionally in complex with any ligand, as encompassed by the claims for those that will yield diffraction-quality crystals.

In view of the overly broad scope of the claims, the lack of guidance and working examples provided in the specification, the high level of unpredictability as evidenced by the prior art, and the amount of experimentation required to make and use all crystals and polypeptides as broadly encompassed by the claims, undue experimentation would be necessary for a skilled artisan to make and use the entire scope of the claimed invention. Applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

[14] Claim(s) 4, 6, and 10 are rejected under 35 U.S.C. 103(a) as being unpatentable over Groenen et al. (*Biochemistry* 36:3826-3836, 1997; "Groenen") in view of Cohen et al. (*J. Med. Chem.* 33:883-894, 1990; "Cohen"), Traxler et al. (*Pharmacol. Ther.* 82:195-206, 1999; "Traxler"), Plowman et al. (*PNAS* 90:1746-1750, 1993; "Plowman-1"), and Plowman (US Patent 5,804,396; "Plowman-2"). The claims are drawn to *in silico* methods for screening ErbB4 inhibitors and testing the selected compounds for inhibitory activity on ErbB4.

The reference of Groenen teaches an EGFR kinase domain homology model and a method for constructing such model (see, *.e.g.,* p. 3827, column 1). According to Groenen, the method of sequence alignment to construct the model as "straightforward" (p. 3827, column 1, middle). Groenen does not teach the use of a model of ErbB4 kinase domain for the use in inhibitor design.

The reference of Cohen teaches methods of identifying molecules that binds to proteins using the three-dimensional structure of the protein, and the commercial

availability of various software packages to be used in said methods. See in particular page 893, right column.

The reference of Traxler teaches ErbB4 (referred to as "c-erbB4" by Traxler) is an EGFR family member and is used as a target for medicinal chemistry programs (p. 195, column 2). Traxler notes that most protein kinases share conserved core structures (paragraph bridging pp. 196-197). Traxler teaches the use of an EGFR homology model toward the successful design of a novel and selective tyrosine kinase inhibitor (p. 195, abstract). Traxler notes that Met769 of the EGFR model interacts with a nitrogen of ATP (p. 198, column 2) and a model of EGFR bound with inhibitor shows a hydrogen bond interaction of the inhibitor with Met769 (p. 199, column 2; p. 203, column 2 and Figure 6).

The reference of Plowman-1 teaches the amino acid sequence of the ErbB4 (referred to as "Her4" by Plowman-1) kinase domain (p. 1748, Figure 1), showing that ErbB4 Met799 corresponds to Met769 of EGFR. Plowman further teaches a method for purifying ErbB4 (p. 1747, columns 1-2).

The reference of Plowman-2 teaches an ErbB4 (referred to as "Her4" by Plowman-2) kinase assay (columns 19-21).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to produce a 3-D model of ErbB4 kinase domain, model potential inhibitors, *e.g.,* the inhibitors as taught by Traxler, into the active site of the model of the ErbB4 kinase domain active site to identify those potential inhibitors that have favorable interaction with active site residues, including Met799, and screen those potential

inhibitors *in vitro* to determine those that inhibit ErbB4 kinase activity. One would have been motivated to do this because Traxler expressly teaches that ErbB4 is a target for medicinal chemistry programs. One would have been motivated to screen for compounds that have favorable interaction with Met799 because: 1) Traxler teaches that EGFR Met769 forms contacts with substrate and inhibitors; 2) EGFR Met769 corresponds to ErbB4 Met799 as shown by Plowman-1; and 3) Traxler teaches that ErbB4 is an EGFR family member and further teaches that most protein kinases share conserved core structures. One would have had a reasonable expectation of success for practicing the above noted method because of the teachings of Groenen, Cohen, Traxler, Plowman-1, and Plowman-2. Therefore, claims 4, 6, and 10, drawn to the method as described above, would have been obvious to one of ordinary skill in the art at the time of the invention.

EXAMINER CLARIFICATION: As noted above, the term “represents” has been broadly, but reasonably interpreted as meaning to serve as an example of something, such that the recited 3-D model serves as an example of an ErbB4 kinase domain – but is not limited to having the structural coordinates of Table 2. Put another way, the claims have been interpreted as meaning that the recited 3-D model is of an ErbB4 kinase domain, wherein the 3-D model is unlimited with respect to the structural coordinates that define the model.

[15] Even if the claims are limited to the structural coordinates of Table 2, the following rejection still applies. Claim(s) 4, 6, and 10 are rejected under 35

U.S.C. 103(a) as being unpatentable over Groenen in view of Cohen, Traxler, Plowman-1, and Plowman-2 and the legal precedent of In re Gulack 217 USPQ 401 (Fed. Cir. 1983). See MPEP §§ 2144 and 2144.04 regarding legal precedent as a source of rationale for rejection under 35 U.S.C. § 103. The claims are drawn to a method as noted above.

The relevant teachings of the references of Groenen, Cohen, Traxler, Plowman-1, and Plowman-2 are set forth above. The combination of references teaches all limitations of the claims with the exception of the structural coordinates of Table 2.

In *Gulack,* the Court held that nonfunctional descriptive material in a claim does not distinguish the prior art in terms of patentability. The key factor in analyzing the obviousness of these claims over the prior art is the determination that the computer algorithm used to identify compounds that inhibit ErbB4 is a known algorithm and is unmodified. If the difference between the prior art and the claimed invention as a whole is limited to descriptive material stored on or employed by a machine, it is necessary to determine whether the descriptive material is functional descriptive material or nonfunctional descriptive material.

The specification discloses (pp. 31-32), "The method of ErbB4 inhibitor design of the present invention includes as a first step: generating a three dimensional computer model which represents a ErbB4 kinase domain in liganded form, said kinase domain being described by the amino acid sequence of SEQ ID NO:1 and having the structural coordinates of Table 2. Typically, such a computer model of SEQ ID NO:1 and the structural coordinates of Table 2 is constructed utilizing a commercially available

software program. Software programs for generating three-dimensional graphical representations of molecules or portions thereof from a set of structural coordinates are well known and used in the art". In this case, it appears that it is the "software programs" that translate the structural coordinates into a 3-D structure. Thus, it appears that the structural coordinates do not share a functional relationship with the computer upon which they are stored. As such, the Table 2 data is considered to be non-functional descriptive material. It is further noted that, as acknowledged by the specification at pp 31-32, the claimed method uses a known, unmodified computer algorithm. Data, which are fed into a known algorithm whose purpose is to compare or modify those data using a series of processing steps, do not impose a change in the processing steps and are thus nonfunctional descriptive material. A method of using a known comparator for its known purpose to compare data sets does not become nonobvious merely because new data becomes available for analysis. Nonfunctional descriptive material cannot render nonobvious an invention that would have otherwise been obvious.

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to practice the screening method as suggested by Groenen, Cohen, Traxler, Plowman-1, and Plowman-2 to identify a compound that inhibits ErbB4, wherein only non-functional descriptive material is additionally present in the claims, which, according to *In re Gulack,* do not distinguish the claimed methods from those taught by the cited prior art references. One of ordinary skill in the art would have been motivated to practice the method suggested by Groenen, Cohen, Traxler, Plowman-1, and Plowman-2 because of the teachings of Traxler and Plowman-1 and would have

had a reasonable expectation of success for practicing the claimed methods because of the teachings of Groenen, Cohen, Traxler, Plowman-1, and Plowman-2. Therefore, claims 4, 6, and 10 would have been obvious to one of ordinary skill in the art at the time of the invention.

Conclusion

[16] Status of the claims:

Claims 4, 6, and 10-14 are pending.

Claims 11-14 are withdrawn from consideration.

Claims 4, 6, and 10 are rejected.

No claim is in condition for allowance.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to David J. Steadman whose telephone number is 571-272-0942. The examiner can normally be reached on Monday to Friday, 7:30 am to 4:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen Kerr Bragdon can be reached at 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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